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Christopher A. Klein, Esq.  
Bristol-Myers Squibb Company  
Post Office Box 4000  
Lawrenceville-Provinceline Road  
Princeton, NJ 08543-4000

EXAMINER

JIANG, DONG

ART UNIT PAPER NUMBER

1646

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/932,145

Applicant(s)

FEDER ET AL.

Examiner

Dong Jiang

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 4/16/04 and 6/17/04.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 30-49 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 30-49 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 1/4/02, 12/23/02, 9/17/03, 1/16/04  
4/16/04
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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### **DETAILED OFFICE ACTION**

Applicant's preliminary amendment and election without traverse of Group III invention, represented by the original claims 12-20, filed on 17 September 2003, and resubmitted on 16 April 2004 are acknowledged. Following the amendment, the original claims 1-29 are canceled, and the new claims 30-49 are added.

Applicant's second preliminary amendment filed on 17 June 2004 is acknowledged. Following the amendment, claims 32 and 34 are amended.

Currently, claims 30-49 are pending and under consideration.

#### **Formal Matters:**

##### ***Priority***

If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. \_\_\_\_" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the

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date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

***Priority determination***

This application claims priority to US provisional applications 60/226,411 and 60/261,779. For the following reasons, the Examiner finds that the present claims 30-49 are not supported in the manner required by 35 U.S.C. 101 and 112, first paragraph by the prior applications, thus the present claims are entitled to the benefit of the filing date of the prior applications.

The priority applications merely discloses the polynucleotide of SEQ ID NO:2, and the encoded polypeptide of SEQ ID NO:4, and indicates that it is a imidazoline receptor homolog (IMRRP1b) based on sequence homology. The prior applications fail to provide any specific and substantial utility directly associated with IMRRP1b, and provides no guidance or working examples to teach how to used the claimed invention. Therefore, the Examiner is not able to establish that the priority document satisfies the utility/enablement requirement of 35 U.S.C. 101/112, first paragraph. As such, the present claims 30-49 are not entitled to the benefit of the filing date of prior applications listed above.

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### ***Specification***

The specification is objected to for the following reasons, appropriate correction is required.

At page 13, lines 9-12, it is indicated that Figure 6 shows a comparison of the FL1-18 cDNA (SEQ ID NO:1 according to the specification, page 4, lines 9-12) to that of the partial clone found in the Incyte database (clone 2499870), which revealed that at nucleotide position 1725 of the Incyte clone a small insertion of 25 bases occurs and at position 3375 of clone FL1-18 an insertion of 47 bases occurs. However, SEQ ID NO:1 only has 2475 nucleotides.

At page 13, lines 12-13, it is indicated that an alignment of the two DNA sequences, FL1-18 (SEQ ID NO:1) and Incyte 2499870 is shown in Figure 8. However, the sequences of Figure 8 are not DNA sequence, they are amino acid sequences.

### ***Claims***

Claim 30 is objected to for encompassing a non-elected subject matter, an antisense polynucleotide (part (c)), which is an invention independent or distinct from the invention originally claimed for the reasons below. The applicant is required to amend the claims to read only upon the elected invention.

The polynucleotide of the elected Invention III, represented by the original claims 12-20, is related to the antisense polynucleotide of claim 30 as they are complementary to each other. However, they are partentably distinct each from the other because the polynucleotide of Invention III is not required for the antisense of claim 30, and they are used in materially different processes, and are for different purposes. The arts for antisense therapy and recombinant production of proteins are separated and distinct, and require non-coextensive searches.

### **Objections and Rejections under 35 U.S.C. §101 and §112:**

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

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Claims 30-49 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 30-49 are directed to an isolated nucleic acid having SEQ ID NO:2 or encoding a polypeptide of SEQ ID NO:4, variants thereof, a vector comprising the nucleic acid, a host cell thereof, and a method of recombinantly producing the polypeptide encoded by the nucleic acid. The encoded polypeptide is designated imidazoline receptor related protein 1b (IMRRP1b).

The specification discloses a nucleic acid comprising a nucleotide sequence of SEQ ID NO:2, and encoding a polypeptide, IMRRP1b, having an amino acid sequence SEQ ID NO:4. Further, the specification asserts that the nucleic acid, the polypeptide encoded thereby and antibodies are useful in diagnosis and treatment of disorders associated with aberrant regulation of blood pressure, induction of feeding, stimulation of firing of locus coeruleus neurons, and stimulation of insulin release, and other disorders (page 3, the last two paragraphs). However, the asserted utility for the IMRRP1b is based on that for the known imidazoline receptor (IMR) as the two molecules share sequence homology (page 2, lines 4-6, and page 45, lines 11-15), and no specific functional activity or biological significance directly associated with either the nucleic acid or the encoded polypeptide IMRRP1b is ever disclosed in the specification.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a known protein. For example, in the transforming growth factor (TGF) family, Vukicevic et al. (1996, PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF- $\beta$  family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF- $\beta$  family members BMP-2 and TGF-1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). Additionally, IL-18 receptor (IL-18R) was thought to be another IL-1 receptor (IL-1R) base on the sequence homology, and therefore, designated IL-1 receptor-related protein (IL-1Rrp) when it was first discovered, and its ligand was unknown (Parnet et al., J. Biol. Chem., 1996, 271(8): 3967-70). IL-1Rrp is now known as IL-18R, has distinct ligand, and possesses distinct function from IL-1R even though it is a member of IL-1R family. In the instant case, the specification fails to disclose any specific functional activity or biological significance directly associated with either the claimed nucleic acid or the encoded polypeptide IMRRP1b. An established utility for the known IMR cannot be

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automatically applied to IMRRP1b without functional analysis. In fact, it is not even clear whether the IMRRP1b would bind the same ligands as that for IMR. While it is likely that IMR and the IMRRP1b may belong to the same family, that by itself does not suggest a utility for the IMRRP1b for the reasons above.

In *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sup. Ct., 1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to a nucleic acid encoding a polypeptide, which has undetermined function or biological significance. Until some actual and specific activity can be attributed to the polynucleotide or polypeptide identified in the specification as IMRRP1b, the claimed invention is incomplete.

Further, according to MPEP, a *substantial* utility is a utility that defines "real world" use, and a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use is not a substantial utility. In the instant case, the IMRRP1b shares sequence homology with IMR, which, at the most, is an invitation for further research and experimentation in order to define or confirm the specific functional activity or biological significance of the IMRRP1b, and to determine the "real world" use. These further research and experimentation, however, is part of the act of invention, and until it has been undertaken, the claimed invention is not considered substantial.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 30-49 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, *even if* there were utility and enablement for the IMRRP1b of SEQ ID NO:4, enablement would not be commensurate in scope with claims 42-46, which encompass % variants (claims 42-45) and hybridization variants (claim 46) of the nucleic acid encoding SEQ ID NO:4.

The specification merely discloses *one* nucleic acid of SEQ ID NO:2 encoding a human IMRRP1b having SEQ ID NO:4, and provides neither information about the structural and functional relationship within the claimed sequence (SEQ ID NO:2) as to which regions of the claimed polypeptides would be tolerant of modification and which would not regarding to retaining the functional activities of the polypeptide, nor guidance or working example of the nucleic acid variants less than 100% identical to SEQ ID NO:2 to teach a commensurate number of the claimed species. Therefore, it is less predictable that any randomly selected variant 80% identical to SEQ ID NO:2 or the hybridization variants would encode a functional protein.

Further, with the limitation of “modulating *cellular development*”, the claims encompass variants that meet the sequence limitation of the claims (% and hybridizing), but may have completely different functional activity from that of the IMRRP1b as “cellular development” can mean many distinct activities, some of which may have nothing to do with the specific function of the IMRRP1b.

Furthermore, claims 42 and 46 recite a functional limitation of “capable of *modulating* cellular development”, and the term “modulating” can be interpreted as either stimulating or inhibiting, which are mutually exclusive, and both cannot be true. The specification does not specify how the IMRRP1b polypeptide “modulates” cellular development in either way, and thus, such a functional limitation is not enabled. Undue experimentation would be required in order to use the claimed invention in its full scope.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 is indefinite for the recitation of “the complimentary sequence (antisense) of ...” as it is unclear whether “the complimentary sequence” is the same as “antisense”, or “antisense” in the parentheses is a part of the limitation of “the complimentary sequence”. The metes and bounds of the claim, therefore, cannot be determined. Further, if the antisense is intended, the claim would be subjected to a further restriction requirement as the antisense sequence is a patentably distinct invention from the elected nucleic acid for the reasons above, and would be withdrawn from consideration.

Claim 41 recites the limitation “*said* heterologous polypeptide”. There is insufficient antecedent basis for this limitation in the claim.

Claims 42 and 46 are indefinite for the recitation of “modulating *cellular development*” as it is unclear what it is intended.

Further, claim 46 is incomplete for omitting essential elements. The claim is limited by a hybridization method under stringent conditions. However, the claim does not recite the washing temperature, which is one of the most important parameters determining the stringency. Without knowing what washing temperature is intended under said stringent conditions, one can not determine the metes and bounds of nucleic acids within the limitations of the claim.

Claims 47-49 are incomplete for depending on the claims that do not exist, i.e., there are no claims 50-52 in the instant application.

The remaining claims are rejected for depending from an indefinite claim.

**Rejections Over Prior Art:**

**The following rejections under 35 U.S.C. § 102 are made in view of the determination that the effective filing date for the instantly claimed invention is 8/17/2001, which is the actual filing date of the instant application.**

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 46 is rejected under 35 U.S.C. 102(b) as being anticipated by Sulston et al. (Locus AC009955, GenEmbl, 09 September 1999).

Sulston discloses a polynucleotide sequence of a human genomic clone, which comprises the sequences of the most of the coding region (exons) for SEQ ID NO:4 of the present invention, i.e., sequences encoding amino acids 17 to 1099 of SEQ ID NO:4 (1-1099) with more than 98% sequence identity (see computer printout of the search results). The cited sequence would hybridize under stringent conditions to a polynucleotide encoding SEQ ID NO:4 as 20 out of 23 exons have 100% sequence identity to that encoding amino acids 101-789 of SEQ ID NO:4. Further, Waterston's polynucleotide would produce the polypeptide having amino acids 17-1099 of SEQ ID NO:4 when it is transfected and expressed properly, which would be expected to be capable of "modulating cellular development" as SEQ ID NO:4 because the encoded polypeptide would have more than 98% of the sequence of SEQ ID NO:4 with about 99% sequence identity to the corresponding regions of SEQ ID NO:4. The reference, therefore, anticipates the present claim 46.

Claim 46 is rejected under 35 U.S.C. 102(e) as anticipated by being Rosen et al., US 2002/0042386 A1.

Rosen discloses a nucleic acid (SEQ ID NO:149), which has 860 nucleotides, comprises nucleotides 1339-2158 of the present SEQ ID NO:2 with 97.6% sequence similarity, and encodes amino acid residues 448-717 of the present SEQ ID NO:4 with 96.3% sequence similarity (see computer printout of the search results). Further, Rosen teaches that said nucleic acid encodes a polypeptide (SEQ ID NO:414), and is expressed in tissues/organs including liver,

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prostate, microvascular endothelial cells, bone marrow cell line, and T cells (Table 1 at pages 36-37; and Table 4 at pages 77, 78, and 80-82), indicating the involvement of "cellular development". As such, Rosen's nucleic acid of SEQ ID NO:149 anticipates the present claim 46 as being a nucleic acid that hybridizes under stringent conditions to a polynucleotide encoding SEQ ID NO:4, and encodes a polypeptide capable of modulating cellular development.

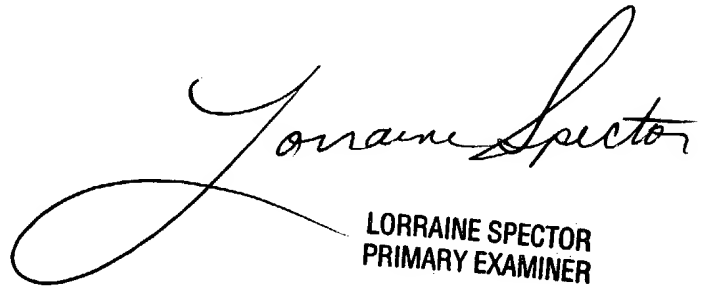
**Conclusion:**

No claim is allowed.

**Advisory Information:**

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.



LORRAINE SPECTOR  
PRIMARY EXAMINER

Dong Jiang, Ph.D.  
Patent Examiner  
AU1646  
6/29/04